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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,796	JACKOWSKI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *3-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4, 11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Preliminary amendment of Paper No. 5, filed on April 23, 2002 has been entered only in part, which relates to claims. Amendment to the specification has not been entered because it is not in compliance with 37 CFR § 1.121.

§ 1.121 "Manner of making amendments in application" states that

(a) Amendments in applications, other than reissue applications . Amendments in applications, other than reissue applications, are made by filing a paper, in compliance with § 1.52, directing that specified amendments be made.
(b) Specification other than the claims and listings provided for elsewhere (§ § 1.96 and 1.825) .—
(1) Amendment by instruction to delete, replace, or add a paragraph. Amendments to the specification, other than the claims and listings provided for elsewhere (§§ 1.96 and 1.8 25), may be made by submitting:
(i) An instruction, which unambiguously identifies the location, to delete one or more paragraphs of the specification, replace a deleted paragraph with one or more replacement paragraphs, or add one or more paragraphs;
(ii) Any replacement or added paragraph(s) in clean form, that is, without markings to indicate the changes that have been made; and
(iii) Another version of any replacement paragraph(s), on one or more pages separate from the amendment, marked up to show all the changes relative to the previous version of the paragraph(s). The changes may be shown by brackets (for deleted matter) or underlining (for added matter), or by any equivalent marking system. A marked up version does not have to be supplied for an added paragraph or a deleted paragraph as it is sufficient to state that a particular paragraph has been added, or deleted.

Specifically, Applicant failed to identify the location of the replacement paragraph and further failed to provide the full text of the amended paragraphs containing sequence identifiers.

Appropriate action is required.

Election/Restrictions

2. Applicant's election with traverse of Group I in Paper No. 10 is acknowledged. The traversal is on the ground(s) that because SEQ ID NOS: 1-6 are fragments of fibronectin

precursor protein, they are identified as markers predictive of type II diabetes, thus, they share a common utility and common structural feature and, therefore, claims 1, 18, 29, 30, 33, 34 and 38 are proper Markush claims. These arguments have been found to be persuasive in part. The Examiner acknowledges that because polypeptides of SEQ ID NOS: 1-6 are asserted to be indicative of type II diabetes and, therefore, share a common utility, the objections to the claims 1, 18, 29, 30, 33, 34 and 38 as being improper Markush claims is withdrawn. However, with the exception of SEQ ID NO: 1 and 4, each of the recited sequences represents a non-overlapping fragment of a larger sequence and each fragment could be embedded within other patentably distinct proteins, a separate search is required for each possible fragment, the restriction is still deemed proper. Fragment of SEQ ID NO: 4 is included within invention of Group I because SEQ ID NO: 1 is a fragment of SEQ ID NO: 4.

Applicant's argument regarding examination of "six short amino acid sequences, four sequences less than the ten sequences normally considered by the Office as reasonable for examination purposes" (middle at page 3 of the Response) has been fully considered but is not deemed to be persuasive for the following reasons. MPEP 804.03 is directed to nucleotide sequences, in which the Commissioner authorized a partial waiver of restriction practice, allowing the examination of up to ten sequences. This waiver was issued in 1996. Since then, the nucleic acid and protein databases that must be searched for each of the independent and distinct sequence claimed herein have multiplied many fold in size, such that it is now burdensome to search more than a single sequence in an application. Further, the waiver allowed, but did not require the Examiner to search ten sequences. Also, the waiver was directed

to nucleotide sequences and not amino acids sequences, which is the case in the instant application.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Claims 1 and 2, in so far as they are directed to SEQ ID NO: 1 and SEQ ID NO: 4 are under examination in the instant office action.

3. The reference cited in Paper No. 10 has only been considered in so far as it supports Applicant's arguments contained therein. If Applicant wishes this reference to be considered in its entirety, Applicant needs to submit the reference in a form of proper IDS in accordance with 37 CFR § 1.97.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1 and 2 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims fail to include any limitations, which would distinguish the claimed polypeptide sequences from those, which occur in nature. In the absence of the hand of man, naturally occurring nucleic acid molecules and proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, mere purity of a

naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui, 156 USPQ 426 (1966). However, when purity results in a new utility, patentability is considered. Merck Co. v. Chase Chemical Co., 273 F. Supp. 68 (1967). Filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the specification, is suggested to obviate this rejection. Applicant should point to the basis in the specification for any amendment to the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Claim 1 is broadly drawn to a biopolymer marker of SEQ ID NO: 1 or SEQ ID NO: 4 or at least one analyte thereof useful in indicating at least one particular disease state. Claim 2 encompasses the biopolymer marker of SEQ ID NO: 1 or SEQ ID NO: 4 or at least one analyte thereof as being predictive of type II diabetes. However, the instant specification fails to provide any guidance on how to use the disclosed polypeptides of SEQ ID NO: 1 or SEQ ID NO: 4 or analytes thereof as a marker or indicator of any disease state, including type II diabetes. There is no information disclosed in the instant specification, which would provide evidence or sound scientific reasoning that a biopolymer marker, which is a polypeptide of SEQ ID NO: 1 or SEQ

ID NO: 4 or an analyte thereof, is specifically associated with any particular disease state in general or is being predictive of type II diabetes in particular, thereby requiring undue experimentation by a skilled artisan to discover how to make and use Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

The nature of the invention is the finding of the specific fragments of fibronectin precursor protein, which are polypeptides of SEQ ID NOS: 1-6, in a serum sample treated according to a protocol provided on pages 40-46 of the instant specification. These fragments were asserted to be "related to Type II diabetes" (page 47, line 2 of the instant specification). The state of the art is such that it does not recognize any specific association of the polypeptide of SEQ ID NO: 1 or SEQ ID NO: 4 with any particular disease state in general or with type II diabetes in particular. Therefore, in the absence of information in the prior art, a skilled artisan would have to solely depend on the instant disclosure to practice the claimed invention. However, the instant specification provides no information on how the detection of a peptide of SEQ ID NO: 1 or of SEQ ID NO: 4 can be used in detecting any particular disease state. Note that although the "disease state" is not limited to a particular disease state, with regard to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the

claims recite and what the claims mean as a whole. In addition, when analyzing the enablement scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. As such, the broadest reasonable interpretation of the claimed invention is such that detection of a peptide of SEQ ID NO: 1 or 4 or an analyte thereof is indicative of "a disease state" vs. non-diseased state. The instant specification fails to provide any evidence or sound scientific reasoning that detection of a biopolymer marker of SEQ ID NO: 1 or 4 or at least one analyte thereof is indicative of "a disease state". Moreover, according to the instant specification, an "analyte" is defined as "any atom and/or molecule; including their complexes and fragment ions" (page 6, lines 15-19). The instant specification, as filed, does not disclose how to use an "atom and/or molecule" as a biopolymer marker for "a disease state".

Furthermore, the instant specification fails to explain the relationship between a polypeptide of SEQ ID NO: 1 or SEQ ID NO: 4 and a "particular disease state". The text on page 47 states that "Figures 1 and 3 are photographs of a gel indicative of the presence/absence of the marker in disease vs. control and, in cases where the marker is always present, the relative strength, e.g. the up or down regulation of the marker relative to categorization of disease state is deduced". While it is not necessary that Applicant understands or discloses the mechanism by which the invention functions, in this case, in the absence of such an understanding the following questions must be answered. Is it "the up or down regulation of the marker relative to categorization of disease state"? Or is "the presence/absence" of the polypeptide of SEQ ID NO: 1 or the polypeptide of SEQ ID NO: 4 indicative of a disease? What is the critical level of up or down regulation that is predictive of a disease state or predictive of type II diabetes?

Thus, Applicant's invention is predicated on the finding that a serum sample being processed according to the disclosed protocol contains polypeptides of SEQ ID NO: 1 and SEQ ID NO: 4. Applicant further extrapolates this result into an assertion that a protein of SEQ ID NO: 1 or of SEQ ID NO: 4 can be used as a marker for type II diabetes or for any disease state in general. Accordingly, it would appear that Applicant provides a single finding (the finding), and then presents an invitation to experiment to determine if polypeptides of SEQ ID NO: 1 and 4 can be used in indicating at least one particular disease state. The text on page 11, third paragraph, states that "a biopolymer marker which is strongly present in a normal individual, but is down-regulated in disease is predictive of said disease; while alternatively, a biopolymer marker which is strongly present in a disease state, but is down-regulated in normal individuals, is indicative of said disease state. Biopolymer markers which are present in both disease and normal states are indicative/predictive based upon their relative strengths in disease vs. normal, along with the observation regarding when their signal strengthens/weakens relative to disease manifestation or progression". Based on this information, a skilled artisan would have to resort to substantial amount of undue experimentation to determine if a marker of SEQ ID NO: 1 or of SEQ ID NO: 4 is absent or present or strongly present in a normal individual, or is up- or down-regulated in disease.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere

germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one can not follow the guidance presented therein and use the claimed biopolymer marker without first making a substantial inventive contribution to discover how to use Applicants' invention as currently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 1 is vague and indefinite because it is not clear whether "analyte thereof" refers to a biopolymer marker or to SEQ ID NO: 1 or 4. According to the instant specification, "biopolymers" are defined as "biological molecules/macromolecules" and an "analyte" is defined as "any atom and/or molecule; including their complexes and fragment ions" (page 6, lines 15-19). Thus, the definitions of these two terms appear to be conflicting, because one would not recognize an atom as a biopolymer. Clarification is required.

7. Claim 2 is indefinite for being dependent from an indefinite claim.

Conclusion

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative

number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
June 9, 2003